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M is a transition metal ion;

the A-Y-B moiety is acetylene;

X and X₁ are co-ligands and wherein at least one of X and X₁ is present; and

Z is a nucleic acid moiety.

47. A compound according to claim 46, wherein said nucleic acid moiety comprises a nucleic acid analog.--

REMARKS

Claims 26-47 are pending. Claims 44-47 are newly added. Support for new claims 44-47 is found on pages 11-12.

The applicants thank the Examiner for his helpful comments.

Claims 26-43 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctively claim the subject matter which applicant regards as the invention.

Claim 26 is rejected for the recitation of the term "A and B are selected from carbon or nitrogen, Y is a bond, and". The applicants thank the Examiner for his helpful suggestion. The amended claim does not recite this term; thus the rejection of record should be withdrawn.

Claim 26 is rejected for containing an improper Markush group. The amended claim recites a correctly formed Markush group and the members of the group are correctly presented. The term "alkene" is deleted and substituted by "acetene". Support for "acetene" derivatives of the compound claimed can be found on page 7, line 8 and page 22, line 18. The terms acetene and ethylene (an alkene, also named ethene) are synonymously

used in, e.g., Grant & Hackh's Chemical Dictionary, 5th edition (eds. R. Grant & C. Grant; McGraw-Hill Book Company, 1987; see pages 5, 220 and 224), a copy of which is enclosed as Exhibit A. Support for "imine" derivatives is found on page 7, lines 9-10 and 17.

Claims 26 and 27 are rejected for the recitation of the term "X and X₁ are co-ligands and wherein at least one of X and X₁ is present;" as being indefinite.

The applicants respectfully remind the Examiner that an applicant may be his or her own lexicographer, defining terms as he or she wishes (see Intellicall, Inc. v. Phonometrics, Inc., 21 USPQ 2d 1383 (Fed. Cir. 1992)). 35 U.S.C. §112, second paragraph, requires the claims particularly pointing out and distinctively claiming the subject matter which the applicant regards as his invention. Applicants respectfully point out that page 8, line 15 to page 9, line 3 of the specification states that:

Suitable ligands are well known in the art and include, but are not limited to, NH₂; pyridine; pyrazine; isonicotinamide; imidazole; bipyridine and substituted derivatives of bipyridine; phenanthrolines, particularly 1,10-phenanthroline (abbreviated phen) and substituted derivatives of phenanthrolines such as 4,7-dimethylphenanthroline and the compounds disclosed herein; dipyridophenazine; 1,4,5,8,9,12-hexaazatriphenylene (abbreviated hat); 9,10-phenanthrenequinone diimine (abbreviated phi); 1,4,5,8-tetraazaphenanthrene (abbreviated tap); 1,4,8,11-tetra-azacyclotetradecane (abbreviated cyclam). In some embodiments, porphyrins and substituted derivatives of the porphyrin family may be used.

The applicants submit that one of skill in the art is well familiar with the term "ligand" as it relates to transition metal complexes. See for example the definition of ligand, page 337, in Grant & Hackh's Chemical Dictionary, McGraw Hill Book Company, 1987 (a copy of which is enclosed as Exhibit B). See also Chapter 2, Introduction to Ligands and Complexes, in Advanced Inorganic Chemistry, Fifth Ed., Cotton & Wilkinson, John Wiley & Sons, 1988, pp 35-83 (a copy of which is enclosed as Exhibit C; see particularly the first sentence of page 36).

The applicants respectfully remind the Examiner that the standard for §112 enablement is that one skilled in the art would be able to make and use the description of the invention to make and use the claimed invention without undue experimentation. "An inventor need not, however, explain every detail since he is speaking to those skilled in the art." DeGeorge v. Bernier, 226 USPQ 758, 762 (Fed. Cir. 1985).

Accordingly, the applicants submit that the term "ligand" is not indefinite as the term is well understood by those in the art. Thus, the rejection of record should be withdrawn.

Claims 26 and 27 are rejected for the recitation of the terms "alkyl", "substituted alkyl", "aromatic group" and "substituted aromatic group" for being indefinite. The applicants point out that the specification fully defines these terms at page 9, line 7 to page 10, line 11:

By "aromatic" or "aromatic group" herein is meant aromatic and polynuclear aromatic rings including aryl groups such as phenyl, benzyl, and naphthyl, naphthalene, anthracene, phenanthroline, heterocyclic aromatic rings such as pyridine, furan, thiophene, pyrrole, indole, pyrimidine and purine, and heterocyclic rings with nitrogen, oxygen, sulfur or phosphorus. Preferred aromatic groups include phenyl groups, pyridine, purine, and pyrimidine groups.

By "substituted aromatic group" herein is meant that the aromatic moiety to which the 1,10-phenanthroline is attached contains further substitution moieties. That is, in addition to the phenanthroline derivative, the aromatic group may be further substituted by any number of substitution moieties. The substitution moiety may be chosen from a wide variety of chemical groups, or biological groups including amino acids, proteins, nucleosides, nucleotides, nucleic acids, carbohydrates, or lipids. That is, any group which contains an aromatic group may serve as the substituted aromatic group. Suitable chemical substitution moieties include, but are not limited to, alkyl, aryl and aromatic groups, amino, nitro, phosphorus and sulfur containing moieties, ethers, esters, and halogens. In some embodiments, as is more fully described below, the substitution moiety of the aromatic group is acetylene linked 1,10-phenanthroline of Structure 2, i.e. two or more 1,10-phenanthrolines share a single Z group, creating multimers and polymers (including dendrimers) of Structure 2.

By "alkyl group" or grammatical equivalents herein is meant a straight or branched chain alkyl group, with straight chain alkyl groups being preferred. If branched, it

may be branched at one or more positions, and unless specified, at any position. The alkyl group may range from about 1 to 20 carbon atoms (C1 -C20), with a preferred embodiment utilizing from about 1 to about 15 carbon atoms (C1 -C15), with about C1 through about C10 being preferred, although in some embodiments the alkyl group may be much larger. Also included within the definition of an alkyl group are cycloalkyl groups such as C5 and C6 rings, and heterocyclic rings with nitrogen, oxygen, sulfur or phosphorus.

By "substituted alkyl group" herein is meant an alkyl group further comprising one or more substitution moieties, as defined above.

The applicants submit that these terms are not indefinite. The examples of "aromatic group", substituted aromatic group", "alkyl group" and "substituted alkyl group" listed in the specifications are known to those in the art. It is clear from reading the specification that each of the listed moieties can be used as "Z". It is also proper to use Markush group claim drafting in reciting members as being selected from the group consisting of alkyl, substituted alkyl, aromatic and substituted aromatic group [see M.P.E.P. 2173.05(h)].

Accordingly, the applicants submit that these terms are not indefinite. However, in the interest of furthering prosecution these terms have been defined to indicate what group of compounds are included within each term. Thus, the rejection of record should be withdrawn.

The Examiner states that in claim 28 the Markush group is grammatically and technically incorrect because the substituent moieties must by definition be "radicals derived from" and are typically claimed in the singular (e.g., a nucleosidyl moiety). Applicants have incorporated Examiner's suggestion into the amended claim which is grammatically correct. There is proper antecedent basis with respect to claims 26 and 27. Claims 29-30, 32-33, 35-36, 38-39, and 41-42 are amended accordingly. Thus the rejection of record should be withdrawn.

Examiner notes that in claim 28, lines 1-3, the term "substituted aromatic group" contains the technical term of art, "aromatic", which requires the presence of a functional

group which contains a cyclic double bonded structure obeying the Hückel $4n+2$ Rule. Examiner further notes that terms included within the Markush group, including "carbohydrates" and "lipids", are not typically defined to include any rings which obey Hückel's Rule. The Applicants do not disagree. However, the Applicants respectfully point out that, as outlined in the specification on page 9, lines 15-28 (see also above on page 9 of this response) and well known in the art, aromatic groups may be substituted with a wide variety of chemical or biological moieties. It is the substitution group that is defined as including a carbohydrate or a lipid; that is, an aromatic group substituted with a carbohydrate or a lipid is what is intended. Claim 28 has been amended to make it clear that it is the substitution group which is defined as including a carbohydrate or a lipid, not the aromatic group. Thus, the rejection of record should be withdrawn.

Examiner notes that in claims 31, 34, 37, and 40, the Markush group members are not properly presented. Without admitting the propriety of the rejection, the claims have been amended according to the Examiner's suggestion and thus the rejection of record should be withdrawn.

Examiner rejects claims 30, 33, 36, 39, 41, and 42 on the basis that the subject matter of the instant claim is indefinite because the attachment point or points have not been defined. As is appreciated by those in the art, attachment can occur at a variety of positions on the nucleosidyl or nucleotidyl moieties. Applicants respectfully draw Examiner's attention to the specification on page 11, line 23 to page 12, line 1 and structures 9-12 which depict the attachment of a 3-acetylene-phenanthroline via the 5 position of the uracil base of a nucleosidyl moiety, a nucleotidyl moiety and a phosphoramidate nucleotidyl moiety. The specification on page 13, lines 7-15 provides for the attachment to other positions on bases, as well as to amino acids and proteins.

Claims 26-43 are rejected under 35 U.S.C. §112, first paragraph. The Examiner has two main points; first, that the specification is not enabling, and secondly that it does not fulfill the written description requirement.

As to the first point, the Examiner agrees that the subject matter directed to substituted nucleosides, substituted nucleotides, substituted nucleoside phosphoramidates and nucleic acid sequences, including substituted nucleosides, is enabling. However, the Examiner appears to question the enablement of other alkyl or aromatic groups.

The applicants respectfully point out that the specification describes the use of palladium-mediated cross coupling reactions to form carbon-carbon bonds between the alkyl and aromatic groups of the invention. As described in the specification at pages 18-19, these reactions are well known in the art. The Applicants submit that these type of reactions have been widely used and, in support of this position, the Applicants respectfully point out that Z groups comprising an aromatic group (Example 3a of Table 1) and 6 substituted aromatic groups (Examples 3b, 3c, and 3d of Table 1 and compounds 7, 8, and 9 of page 32) have been made.

As outlined in M.P.E.P. §2164.04, the Applicants respectfully remind the Examiner that in order to properly reject under §112, first paragraph, the Examiner has the initial burden of establishing a reasonable basis to question the enablement provided for the claimed invention:

A threshold issue is whether the PTO met its burden of proof in calling into question the enablement of appellant's disclosure. This burden required that the PTO advance acceptable reasoning inconsistent with enablement. In re Strahilevitz, 212 USPQ 561, 563 (CCPA 1982); see also In re Marzocchi, 169 USPQ 367, 369 (CCPA 1971).

Accordingly, the Examiner should submit reasons why the original specification does not enable one skilled in the art to make and use the compounds of the present invention

as claimed herein. The applicants submit that the palladium-mediated cross-coupling reactions outlined in the specification can be used to form a wide variety of compounds, and the burden is on the Examiner to show why these well-known general reactions could not be used to add other types of alkyl and aromatic groups, including substituted groups.

As to the written description rejection, unlike the "enablement" requirement, the "written description" requirement of 35 U.S.C. §112, first paragraph is not concerned with support commensurate with the breadth of the claims. The essential purpose of the written description requirement is to show the possession of the invention as of the filing date as a *prima facie* date of invention. In re Smith, 481 F.2d 910, 178 U.S.P.Q. 620,623 (CCPA 1973). Accordingly, the specification is required to contain a statement that adequately describes the invention as claimed. However, the invention need not be described in *ipsis verbis* in order to satisfy the description requirement. See In re Lukach, Olson, and Spurlin, 169 U.S.P.Q. 795, 796 (CCPA 1971). It is sufficient to satisfy the written description requirement if the

specification contains a statement of appellant's invention which is as broad as appellant's broadest claims . . .

In re Robins, 420 F.2d 452, 166 U.S.P.Q. 552, 555 (CCPA 1970).

It is only required, for example, that the specification describe the invention sufficiently for those of ordinary skill in the art to recognize that the applicant invention the subject matter he now claims.

In re Voss, 557 F.2d 812, 194 U.S.P.Q. 267, 271 (CCPA 1977).

In view of the evidentiary function of the written description requirement and the relative ease with which it is met, it is not surprising that description requirement must be found, specifically or inherently, within the specification and original claims.

As outlined in M.P.E.P. §2163.04, the Examiner has the initial burden of presenting evidence or reasons why those of skill in the art would not recognize in the disclosure a description of the invention defined by the claims. This the Examiner has not done, and the rejection should be withdrawn.

Examiner considers claims 26-28 deemed to represent subject matter which would require undue experimentation by the ordinary practitioner to reduce the invention to practice. In addition to the arguments discussed above, applicants respectfully draw Examiner's attention to M.P.E.P. §2164.01 and in In re Wands, 8 USPQ 2d 1400 (Fed. Cir. 1988), the factors for consideration are:

- (1) The quantity of experimentation necessary (time and expense);
- (2) The amount of direction or guidance presented;
- (3) The presence or absence of working examples of the invention;
- (4) The nature of the invention;
- (5) The state of the prior art;
- (6) The relative skill of those in the art;
- (7) The predictability or unpredictability of the art; and
- (8) The breadth of the claims.

All of these factors must be evaluated together; it is not sufficient, as the Examiner has done, to focus on one factor to the exclusion of the others.

As regards the first factor, the quantity of experimentation in the present invention necessary to make the claimed compounds, the applicants submit that the quantity of experimentation is not great. Palladium-mediated cross coupling reactions are well known to be versatile; thus the quantity of experimentation supports a finding of enablement.

As regards the second factor, the amount of direction or guidance presented in the specification is high.

As regards the third factor, the presence or absence of working examples of the invention, the application contains examples of the addition of aromatic groups and substituted aromatic groups. Thus the presence of these working examples supports a finding of enablement.

As regards the fourth factor, the nature of the invention, the invention is directed to the generation and use of 1,10-phenanthroline derivatives substituted at the 3-and/or 8-positions. Once the inventors have shown how to derivatize the 3-and 8-positions, for example with bromine, well-known chemical reactions (palladium reactions) are used to generate the compounds of the invention. Thus the nature of the invention supports a finding of enablement.

As regards the fifth and sixth factors, the state of the prior art and the relative skill of those in the art, the Examiner will understand that both are high, and thus these factors support a finding of enablement.

As regards the seventh factor, the predictability or unpredictability of the art, the invention relates to the generation of a class of phenanthroline compounds. Having shown that 1,10 phenanthroline can be derivatized at the 3-and/or 8-positions, the applicants submit that a wide variety of compounds are enabled.

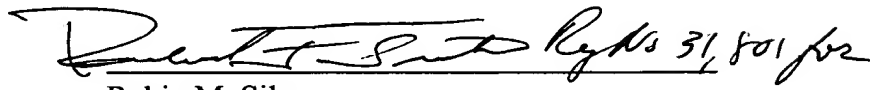
Finally, as regards the breadth of the claims, the claims are directed to a class of compounds comprising derivatized phenanthrolines. The applicants submit that the breadth of the claims support a finding of enablement as well.

Thus, in conclusion, the specification, taken in conjunction with the state of the art at the time the invention was filed, fully enables one of ordinary skill in the art to make and use

the invention without undue experimentation. Thus the Applicants respectfully request reconsideration and withdrawal of the rejection.

The Applicants submit that the claims are now in condition for allowance and an early notification of such is respectfully solicited.

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A handwritten signature in dark ink, appearing to read "Robin M. Silva", is written over a horizontal line.

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